cause was found. The most common obstructive anomalies were valves in the posterior urethra or ureters, stenosis at the ureteropelvic or uretero-vesical orifices, or pressure from an aberrant artery.

3. Inflammatory changes, as recognized by clinical pyuria or by the finding of pus in the urine at autopsy, were present in 25, or 43 per cent, of the cases. Thus, while it would appear that urinary stasis favours infection of the urinary tract, it should be pointed out that 20 of the cases showing obstruction were free from infection. Therefore, the mere fact that examination of the urine is negative, is no proof that the urinary tract is normal.

4. Functional disturbances, as recognized by the complaint of the patient or as revealed by clinical investigation, may be due primarily to the anomaly itself or secondarily to the anatomical changes resulting from obstruction or to a superadded infection.

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GRANULOSA AND THECA CELL TUMOURS OF THE OVARY*

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DURING recent years there has been a marked revival of interest in the clinical and pathological features of solid ovarian tumours. This has been particularly true for those tumours made up of the cellular elements of the Graafian follicle, the granulosa and theca cells. The granulosa cell tumour was first described by von Kahlden[1] in 1895. In 1915 Robert Meyer[2] published a monograph on the subject but clinical interest was not aroused until it was demonstrated that they secreted œstrin. In 1936 it was accidentally discovered that tumours of the granulosa group could be experimentally produced by irradiation of the ovaries of mice.[3] As a result a considerable volume of literature has rapidly accumulated in regard to these tumours in excess of their clinical importance. They do present, however, many characteristics that are of considerable interest to both clinician and pathologist.

Granulosa cell tumours are not common, nevertheless they cannot be classified as rare. Over 250 such growths have been reported, but this certainly does not give a true picture of their frequency, as it is only in recent years that general pathologists have become familiar with their microscopic appearance. In 80 malignant primary ovarian neoplasms Sailer[4] encountered 14 granulosa cell tumours, an incidence of 17.5 per cent, while Schröder, according to Traut,[5] estimated that 2 to 3 per cent of solid ovarian tumours belong to this group. Our incidence, based on 612 ovarian neoplasms of all types, is 2.6 per cent.*

It is difficult to estimate the malignancy of the granulosa cell tumour. Long follow-up records are not common, and recurrences have been reported many years after the removal of the primary tumour. In a series of 54 cases reported by Traut and Marchette[6] 15 per cent were clinically and histologically malignant. We have not as yet had a clinically malignant one although seven of our cases have been followed for five years or longer. The tumour may be malignant regardless of the age of the patient. Anderson and Sheldon,[7] in 1937, reported a malignant tumour in a child of three and a half years of age. The rate of growth varies markedly. One of our patients was observed for a period of three and a half years before operation. During this time only slight if any increase in size of the tumour was evident, while in another case the only complaint was a rapidly enlarging abdomen.

Granulosa cell tumours vary markedly in size. Very small ones a few mm. in diameter have been described as well as huge ones, the largest weighing 34 pounds.[8] They rarely invade through the capsule of the ovary. They as a

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* These cases will be reported in detail in a later publication.

rule are of relatively soft brain-like consistency and vary in colour from pale grey to a distinct yellow, the characteristic colour of the normal corpus luteum. The larger tumours usually show areas of interstitial hæmorrhage, cystic degeneration, and necrosis. Meyer in his original monograph described three microscopic types, the follicular or mature type, the cylindroid, and the sarcomatoid. In most tumours more types than one are evident, and in some all variations of pattern of growth may be seen. The wide variations in both gross and microscopic appearance are well demonstrated by the accompanying photographs of our specimens.

The secretion of œstrin is one characteristic of these tumours which is of particular clinical interest. It results in changes in the endometrium, myometrium, and, in some cases, changes in the breasts and external genitalia. The endometrium, as a result of the prolonged stimulation by œstrin, enters on an unrestricted phase of proliferation ending in hyperplasia of the Schröder or cystic type. Clinically, this results during the years of sexual maturity in periods of amenorrhœa alternating with irregular, prolonged or profuse bleeding. If the tumour occurs before puberty, precocious menstruation results as well as the development of secondary sex characteristics. When it occurs after an established menopause, uterine bleeding recurs, the uterus hypertrophies, and a clinical picture simulating carcinoma of the endometrium is produced. While most tumours secrete sufficient œstrin to cause this chain of symptoms, some do not. In our experience the size of the tumour bears no relationship to its physiological activity.

The granulosa cell tumour is not the only ovarian neoplasm characterized by the secretion of œstrin. In 1932 Loeffler and Priesel[9] described a solid ovarian tumour having the gross appearance of a fibroma and made up of cells microscopically resembling the cells of the theca interna. Just as in the normal Graafian follicle luteinization of the theca occurs, so in these tumours islands of theca cells showing varying degrees of luteinization are evident. The presence of fat in the luteinized cells as well as in the cells not showing this change gives to these tumours their diffuse or streaked yellow colour. The granulosa and theca cell tumours are very closely related and probably have a common origin in the ovarian mesenchyme. Some believe that these two types are one and that the theca cell variety is not an entity. Traut,[6] in a study of 54 examples of the theca and granulosa cell group, showed that most of them were composed of a mixture of both types of cell. Realizing the close relationship between the two, it would seem wise for the present at least to separate them, largely because of the rather distinct gross and microscopic appearance of the theca cell variety.

As previously mentioned, the prolonged effect of the œstrin secreted by granulosa and theca cell tumours results in endometrial hyperplasia and uterine bleeding. The possible relationship between endometrial hyperplasia and carcinoma

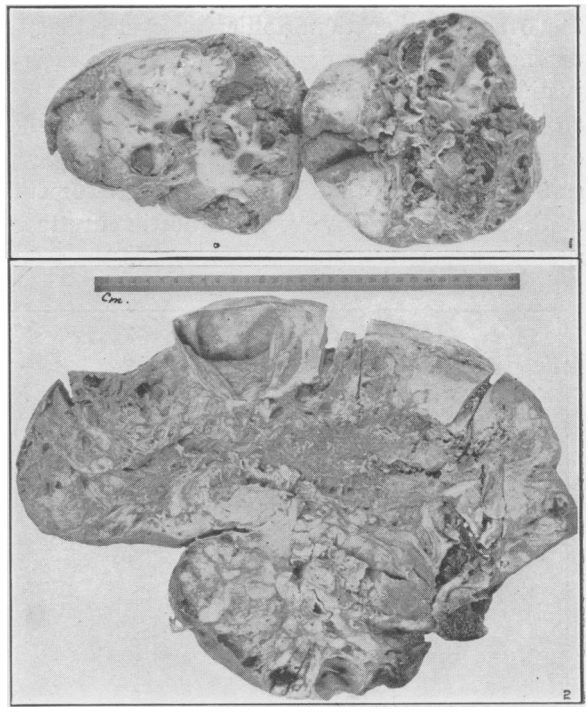

Fig. 1.—Typical granulosa cell tumour, 8 cm. in diameter, showing areas of cystic degeneration and interstitial hæmorrhage. **Fig. 2.**—An unusually large granulosa cell tumour showing extensive cystic degeneration and necrosis.

of the endometrium is being more and more frequently commented upon in gynæcological literature. There is now considerable evidence that the relationship between these two conditions is more than a casual one. In this regard it is interesting to note that three cases of carcinoma of the uterus and granulosa cell tumour of the ovary have been recently reported from the Mayo Clinic.[10] We too have seen this association on more than one occasion with both the theca and granulosa cell variety.

Despite the relatively infrequent occurrence of this group of ovarian neoplasms, they do at

certain age periods produce a chain of signs and symptoms that should in many cases lead to a correct pre-operative diagnosis. The occurrence of uterine bleeding and the development of secondary sex characteristics in a girl before puberty, particularly if other evidence of glandular dyscrasia is absent, are strongly suggestive of granulosa cell tumour. Such a case was reported by Hare,[11] in which rectal examination revealed an ovarian enlargement and a diagnosis of granulosa cell tumour was made and confirmed by operation.

During the period of sexual maturity endometrial hyperplasia and uterine bleeding are so commonly encountered without any change in the ovaries, other than follicular cysts, that a diagnosis of a granulosa cell tumour is rarely justified. When vaginal bleeding occurs after an established menopause, carcinoma of the cervix or the uterus is much more likely to be a cause of bleeding than a granulosa cell tumour of the ovary. If, however, diagnostic curettage reveals endometrial hyperplasia, and at the same time the uterus fails to show the usual post-menstrual atrophy, then a granulosa cell tumour may be present. If an ovarian tumour is palpated as well, the diagnosis is warranted. All patients, however, suffering from post-menopausal bleeding and an ovarian tumour will not have a growth of the granulosa cell type. Papillary and adeno-carcinoma of the ovary occasionally are associated with uterine bleeding and may in some instances metastasize to the endometrium. Frequently granulosa tumours are quite small and cause no appreciable enlargement to the ovary, and yet may be responsible for hyperplasia of the endometrium and bleeding. This naturally brings up the question of the clinical management of cases of post-menopausal uterine hypertrophy and endometrial hyperplasia in the absence of a palpable ovarian tumour. Treatment by either high voltage x-ray or intra-uterine radium should not be employed in such cases. A period of observation after the curettage is indicated, then if the hyperplasia and bleeding recur, even if re-examination

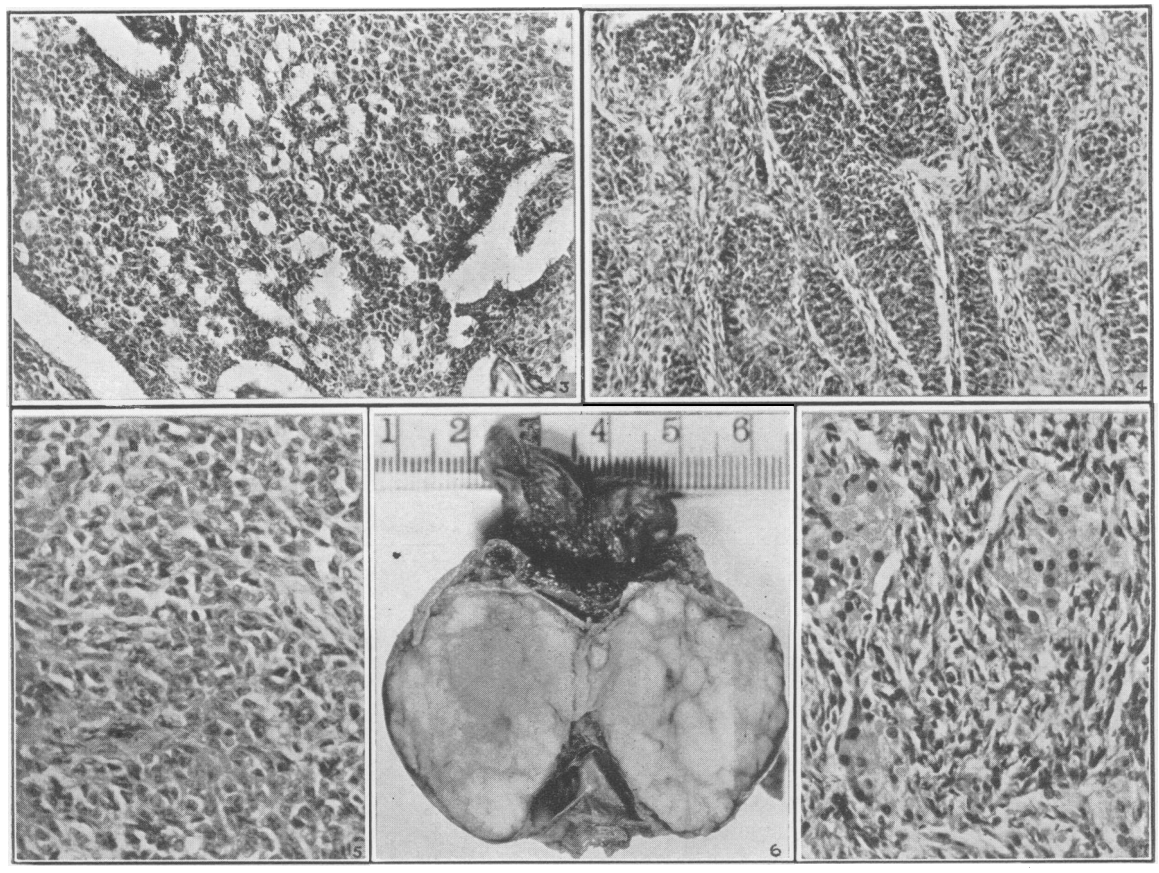

Fig. 3.—Typical microscopic picture of the mature or follicular type of granulosa cell tumour. **Fig. 4.**—Cylindroid type of granulosa cell tumour. **Fig. 5.**—Sarcomatoid type of granulosa cell tumour. **Fig. 6.**—Theca cell tumour having the gross appearance of a fibroma; it was however distinctly yellow in colour. **Fig. 7.**—Photomicrograph of theca cell tumour showing islands of luteinized theca cells.

fails to reveal an ovarian tumour, hysterectomy and bilateral oöphorectomy are justified. It should be emphasized that this radical treatment does not apply to all cases of post-menopausal uterine bleeding when carcinoma of the uterus does not exist, but only to those cases where endometrial hyperplasia and myometrial hypertrophy are present.

The general surgical management of these tumours varies with the age of the patient and the presence or absence of gross evidence of malignancy. When they occur before puberty or during the early years of sexual maturity simple removal of the tumour will usually result in a return of the normal status of the patient. In pre-pubertal years the bleeding stops and breast development temporarily ceases or regresses. During the years of sexual maturity a return to normal menstruation can be expected and even pregnancy may occur. During the menopausal and post-menopausal years hysterectomy and bilateral oöphorectomy should be performed.

If there is gross or microscopic evidence of malignancy, post-operative high voltage x-ray therapy should be used. If, on the other hand, the tumour is small, shows no gross evidence of malignancy, and is of the mature or follicular type, post-operative radiation is probably not necessary. It has been, however, our practice to employ such post-operative radio-therapy in most cases when the tumour occurs at or after the menopause, regardless of clinical or pathological evidence of malignancy.

The experimental production of granulosa and theca cell tumours in mice by irradiation of the ovaries is worthy of consideration by the gynæcologist who so frequently treats bleeding at the menopause by radio-therapy. Whether changes can be produced in the human ovary by radium or x-ray that are in any way comparable to changes in the ovaries of mice at present remains undetermined. When one considers how often radio-therapy is employed in both benign and malignant lesions of the genital tract, one would seem justified in thinking that such tumours would have been reported after radiation if such an occurrence is likely. The experimental evidence, however, is sufficiently striking to warrant caution in the use of this physical agent and restriction of its employment to those cases presenting very definite indications for its use.

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EYELID DISORDER IN TRICHINOSIS.—Trichinosis should be suspected whenever the membrane lining the eyelids presents a waxy-yellow, swollen appearance without known cause, Louis Lehrfeld and Carl F. Breisacher state in the *Journal of the American Medical Association* for November 23, 1940. In their report of a case in which this condition, known as bulbar chemosis, was found due to trichinosis (infestation with worms present in undercooked pork) the authors say that this is a frequent and prominent symptom of trichinosis, and many cases are probably missed by the eye-specialist because the complication has not been kept in mind. They suggest that white blood cell counts be made in all patients who present this characteristic swelling without apparent cause. Infestation with the trichinosis parasites raises this count. Mild cases of trichinosis may not be accompanied by illness and thus the presence of the eye symptom may lead to correct diagnosis. In most of the cases reported, pain on movement of the eyes was present, but in the authors' case such pain did not occur.